REMARKS

The Office Action of May 22, 2002 has been received and carefully reviewed and the foregoing amended claims and the following comments are a complete response thereto.

Claims 1-17, 19-24, 26, 28-30, 32-34, and 37-66 are all the pending claims under examination. By this Amendment, claims 5-12 have been amended to recite proper subject/verb tense. This amendment is only cosmetic and does not change the scope of the claimed subject matter. No new matter has been added, and consideration and entry of the amended claims is requested.

Applicants gratefully acknowledge the Examiner's withdrawal of the following rejections of the claims based on the Amendments filed on October 16, 2001 and January 3, 2002: Claims 1, 3, 15-17, 19, 20, 46, 47 and 58-63 under 35 U.S.C. §§102(b)/ 103(a) over Kuen and Deblaere; and Claims 5-12 under 35 U.S.C. §112, second paragraph.

I. Response to Objections to Claims 5-12

The Examiner has objected to claims 5-12 for lacking subject/verb agreement without pointing out specific examples. The Examiner appears to be referring to the tense of the verb "encode" in these claims and which should more properly recite "encodes".

Applicants have amended Claims 5-12 to recite "encodes" which renders the Examiner's objection moot.

II. R spons to R jection of Claims 1-3, 13, 14 and 59 under 35 U.S.C. § 102

Claims 1-3, 13, 14 and 59 are rejected under 35 U.S.C. § 102 as being anticipated by Miyamoto (FEMS Microbiology Letters, 1994)).

The Examiner considers claims 1-3, 13, 14 and 59 *prima facie* anticipated by Miyamoto.

The Examiner relies upon Miyamoto for teaching a full-length clone for an S-layer protein expressed in E. coli, recombinant phage containing the clone, transfecting E. coli with phage and amplifying the phage, subcloning the gene into plasmid vectors compatible with E. coli, detecting subclones by hybridization methods, and hybridization methods.

The Examiner admits on the record that although Miyamoto does not specifically disclose the sequence of SEQ I.D. No. 1, the S-layer protein "appears to be the same" and thus the claimed nucleotide sequence/amino acid sequence would be inherent to the S-layer gene of Miyamoto.

Applicants traverse the Examiner's rejection of claims 1-3, 13, 14 and 59 over Miyamoto for the following reasons.

Claim 1 is directed to a nucleotide sequence corresponding to SEQ ID NO: 1 encoding the S-layer protein for **Bacillus stearothermophilus, a gram positiv bacterium**.

Miyamoto discloses the nucleotide sequence for the S-layer gene from the **gram negative Campylobacter rectus ATCC 33238** strain. Bacillus and Campylobacter are different bacterial genii and specii. To further substantiate the patentability of the instant invention, enclosed please find a copy of a print-out from the EMBL data bank

disclosing the nucleotide and amino acid sequences for the S-layer protein of Campylobacter rectus (Attachment #1). A detailed comparison of the S-layer gene of C. rectus and the S-layer gene of B. stearothermophilus reveals that the sequences share no homology, and therefore, the instant claimed sequence is not anticipated by Miyamoto.

Applicants also direct the Examiner's attention to the date of deposit for the Miyamoto sequence (March 13, 1997), namely, that being **after** the filing date of the PCT International Application for the present application. Even though Miyamoto teaches a cloned, gram-negative bacterial S-layer gene, the gene sequence is not the same as the claimed gene sequence(s) and the date of deposit post-dates the filing date of the present application; therefore, Miyamoto is not an effective reference under §102(b) with respect to the instant claims.

Claims 2 and 3 are respectively directed to E. coli host cells and isolated forms of an assembled S-layer structure obtained from the interior of the host cell. Miyamoto may teach expression of a recombinant C. rectus S-layer protein in E. coli, but the reference is specifically silent with respect to transforming E. coli with a B. stearothermophilus S-layer gene. Also, Miyamoto does not teach that the C. rectus S-layer protein would be expressed in crystalline, assembled form in the interior of the host cell as for the inventive process. While in Figure 1, Miyamoto explains that the C. rectus surface-layer or "S-layer protein" is normally localized to the exterior cell surface, Miyamoto specifically teaches that the structures of the S-layer protein have not been fully characterized (see, for example, the last sentence under the section entitled

"Results" where Miyamoto states "Further studies...are needed to elucidate the structure and function of the C. rectus surface-layer protein").

Claims 13 and 14 are directed to a nucleic acid encoding a **gram positive signal peptide** corresponding to the signal peptide encoding region of SEQ ID NO 1. Miyamoto's S-layer gene is from a gram negative bacterium and if it contains a signal peptide domain, it should only be a gram negative signal peptide. Miyamoto does not teach engineering a nucleic acid region encoding a gram positive signal peptide into the nucleotide encoding the S-layer protein.

Claim 59 is directed to the hybridization conditions at 55°C. Miyamoto also teaches these stringency conditions for the wash step but not for a Bacillus stearothermophilus-derived S-layer gene.

Applicants have explained the patentably distinguishable features of the present claimed invention over the Miyamoto reference, and have pointed out that the reference is too late to be prior art against this application. Accordingly, withdrawal of the rejection is deemed proper.

III. Response to Rejection of Claims 1-17, 58 and 61 for Obviousness-Type Double Patenting

Claims 1-17, 58 and 61 are rejected by the Examiner for obviousness-type double patenting in view of claims 1, 3, 4, 7, 8, 10 and 12 of Applicants' U.S. Application No. 09/463,402.

Applicants respectfully submit that the instant application and the 09/463,402 application do not share a common assignee as required under MPEP §706.02(l)(2).

Lubitz and Sleytr are assignees for the present application and Lubitz is the sole assignee for the 09/463,402 application. Common ownership is defined as 100 percent ownership by the same assignee, and by definition, this requirement is not met. Accordingly, the obviousness-type rejection is improper and a terminal disclaimer need not be filed. Accordingly, withdrawal of this rejection is deemed proper.

IV. Response to Rejection of Claims 1-17, 19, 20, 46, 47 and 58-65 for obviousness-type double patenting

Claims 1-17, 19, 20, 46, 47 and 58-65 are rejected for obviousness-type double patenting in view of Claims 1, 3, 5, 7, 8, 10 and 12 of Applicants' U.S. Application No. 09/463,402 in view of Deblaere.

Applicants respectfully submit that the instant application and the 09/463,402 application do not share a common assignee as required under MPEP §706.02(l)(2). Lubitz and Sleytr are assignees for the present application and Lubitz is the sole assignee for the 09/463,402 application. Common ownership is defined as 100 percent ownership by the same assignee, and by definition, this requirement is not met. Accordingly, the obviousness-type rejection is improper and a terminal disclaimer need not be filed. Accordingly, withdrawal of this rejection is deemed proper.

CONCLUSION

In view of the foregoing amended claims 5-12, Applicants' arguments for patentability of the claims over Miyamoto, and the Attachment, Applicants submit that

the application is now in condition for allowance, and respectfully request that this application be passed to issuance.

If for any reason, the Examiner determines that the application is not now in condition for allowance, it is respectfully requested that the Examiner contact by telephone the Applicants' undersigned attorney at the indicated telephone number to arrange for an interview to expedite the disposition of this application.

In the event this paper is not being filed, Applicants respectfully petition for an appropriate extension of time. Any fees for such an extension, together with any additional fees, may be charged to Counsel's Deposit Account No. 01-2300, referencing Docket No. 100564-08013.

Respectfully submitted,

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Fax: 202/638-4810
LAB:elp
Enclosures: Marked-Up Copy of Original Claims
Attachment 1 - Printout from EMBL Data Bank

MARKED-UP COPY OF THE CLAIMS FOR 09/117,447

In the claims:

5. (Thrice Amended) The process as claimed in claim 4, wherein the at least one insertion [are] is [selected from the group consisting of] a nucleotide [sequences] sequence encoding a member selected from the group consisting of cysteine residues, regions with several charged amino acids or tyrosine residues, DNA-binding epitopes, metal-binding epitopes, immunogenic epitopes, allergenic epitopes, antigenic epitopes, streptavidin, enzymes, cytokines, and antibody-binding proteins.

6. (Thrice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] encodes streptavidin.

7. (Thrice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] encodes immunogenic epitopes from a herpes virus.

8. (Thrice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] encodes enzymes comprising polyhydroxybutyric acid synthase or bacterial luciferase.

9. (Twice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] encodes cytokines comprising interleukins, interferons or tumour necrosis factors.

10. (Twice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] encodes antibody-binding proteins comprising protein A or protein G.

11. (Twice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] encodes antigenic epitopes which bind cytokines or endotoxins.

12. (Twice Amended) The process as claimed in claim 5, wherein the at least one insertion [encode] <u>encodes</u> metal-binding epitopes.

Attachment #1

USAN 09/117,447
Inventor: Lubitz et al.
Filed: December 2, 1998

Anlage

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ID   AB001876   standard; DNA; PRO; 4450 BP.

AC   AB001876;

SV   AB001876.1

DT   09-OCT-1998 (Rel. 57, Created)
DT   09-OCT-1998 (Rel. 57, Last updated, Version 1)

DE   Campylobacter rectus gene for S-layer protein, complete cds.

KW   S-layer protein.

OS   Campylobacter rectus
OC   Bacteria; Proteobacteria; epsilon subdivision; Campylobacter group;
OC   Campylobacter.

RN   [1]
RP   1-4450
RA   Miyamoto M.;
RT   ;
RL   Submitted (13-MAR-1997) to the EMBL/GenBank/DDBJ databases.
RL   Manabu Miyamoto, Okayama University Dental School, Periodontology and
RL   Endodontology; 2-5-1 Shikata-cho, Okayama 700, Japan
RL   (E-mail:probledo@bu.edu, Tel:81-86-235-6677, Fax:81-86-227-2143)

RN   [2]
RA   Miyamoto M., Maeda H., Kitanaka M., Kokeguchi S., Takashiba S.,
RA   Murayama Y.;
RT   "The S-layer protein from Campylobacter rectus: sequence determination
      and function of the recombinant protein";
RL   FEMS Microbiol. Lett. 166:275-281(1998).

DR   SPTREMBL; O87083; O87083.

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